UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

DN

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/465,747	06/06/95	BROWN C	PAPER 27 CONT

HM12/0219

INTELLECTUAL PROPERTY GROUP
GRAHAM & JAMES LLP
885 THIRD AVENUE, 24TH FLOOR
NEW YORK NY 10022-4834

EXAMINER	
MOSHER, M	

ART UNIT	PAPER NUMBER
1643	27

DATE MAILED: 02/19/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/465,747	Applicant(s) Brown
	Examiner Mosher	Group Art Unit 1643

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *54-57* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *54-57* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1643.

Interference

Interference No. 104,149 has been terminated by a decision adverse to applicant. *Ex parte* prosecution is resumed.

Claims 49-53, as to which judgement adverse to applicant has been rendered, stand finally disposed of in accordance with 37 CFR 1.663. Prosecution of claims 54-57 is resumed.

This replaces the Office action mailed 2/19/97.

Claim Rejections - 35 USC § 112

Claim 54 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for virus-like particles comprising VP1 and VP2, does not reasonably provide enablement for virus-like particles comprising VP1 in the absence of VP2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Young et al (5,508,186) is cited as evidence that VP1 fails to form a virus-like particle in the absence of VP2. See column 11 line 50 to column 12 line 23. Therefore the teachings of the instant specification are seen as inadequate to enable the full scope of the claim, which encompasses particles consisting of VP1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claim 55 is rejected under 35 U.S.C. 102(b) as being anticipated by Ozawa et al (Journal of Biological Chemistry 263:10922-10926, 1988). Ozawa et al teaches B19 capsid proteins VP1 and VP2 which were isolated by synthesis using in vitro translation from an isolated synthetic mRNA, and purified by immunoprecipitation. See page 10923, second column, under "In vitro production of capsid proteins by synthetic B19 transcripts". These proteins meet each and every limitation of the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 54 and 57 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Young et al (5,508,186). Young et al teaches virus-like particles, made by expression of coding sequences in CHO cells. Although the process of making the particles is different from the process recited in these claims, the virus-like particles reasonably appear to have essentially the same characteristics and utility regardless of whether they were produced in mammalian or insect cells. The Patent Office does not have the facilities to compare materials produced by different methods. Therefore, the invention as a whole is seen as prima facie obvious, if not anticipated, by the reference product.

In making the following rejections, claims 54 and 57 are denied the benefit of the filing date of priority application NL 8902301 because the application does not adequately describe or teach how to make virus-like particles as claimed. The NL application discusses virus-like particles which consist of VP1 and VP2, see for example page 4, lines 18-24 and 30-32. The application also discusses "recombinant virus-like particles which consist of VP1 and/or VP2", see for example page 5, lines 30-32. However the application provides no working examples showing production of virus-like particles. The application identifies a preferred method of making particles which consist of VP1 and VP2, using a vector including splice sites so that both products would be produced from a single coding sequence. However, this method is not described in the PCT application. A different method, involving co-infection with two coding sequences, is used in the PCT application. Therefore it appears that the NL application does not describe an effective method to provide a baculovirus expression system which is necessary for expression of both VP1

and VP2 proteins. In addition, the PCT application makes clear that VP2, but not VP1, is capable of forming a virus-like particle. Since the NL application teaches a different, apparently unsuccessful method for making particles containing VP1+VP2, and since the priority application provides no blazemarks to the subunit which is capable of assembling as a virus-like particle, it appears that the priority application lacks a written description or an enabling disclosure for the virus-like particles. The effective date for claims 53, 54, and 57 is therefore September 11, 1990.

Claims 55 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Wood et al with any of Sisk et al, Cotmore et al, or Ozawa et al (T). Wood et al teaches expression of the major immunogenic capsid protein VP2 of canine parvovirus in a baculovirus expression vector system, and teaches that the recombinant protein is immunogenic and protective. This differs from the claimed invention in that the instant claims involve the human B19 parvovirus VP1 or VP2 protein, rather than the canine parvovirus VP2 protein. However, the secondary references teach DNA encoding the VP2 capsid protein of B19 parvovirus, and also teach the overlapping DNA encoding VP1 capsid protein. It would have been within the ordinary skill of the art to substitute known B19 VP2 or VP1 capsid protein coding sequences for the canine VP2 sequence, with reasonable expectation of success in obtaining a similarly antigenic product. The instant claims also differ from Wood et al in requiring isolation and purification of the recombinant product, while Wood et al used whole cells containing the recombinant product. However, isolation and purification of recombinant products was a matter of routine at the time the invention was made, and one of ordinary skill would have been motivated to isolate and purify

the recombinant product for the obvious advantages of purity for use as an antigen. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Claims 54 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kajigaya et al in view of French et al and any of Sisk et al, Cotmore et al, or Ozawa et al (T). Kajigaya et al teaches production of B19 virus-like particles containing VP1 and VP2 by expression of the B19 VP1/VP2 open reading frame in CHO cells. Kajigaya et al also teaches that the particles can be used in immunofluorescence and ELISA assays. This differs from the claimed invention in that Kajigaya et al did not use a baculovirus expression system. However, French et al teaches production of particles by coexpression of two viral proteins in a baculovirus recombinant, with the particles having the correct, nonequivalent amounts of the two viral proteins. Sisk et al, Cotmore et al, and Ozawa et al all teach DNAs encoding the VP1 and the VP2 products. It would have been within the ordinary skill of the art to use a baculovirus expression system to coexpress the VP1 and VP2 coding sequences taught by Sisk et al, Cotmore et al, or Ozawa et al, using a baculovirus coexpression system as taught by French et al for another type of two-component particle, with reasonable expectation of success. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Response to Amendment

The declaration by Dr. Spaan has been considered. Dr. Spaan argues that Cotmore et al and Sisk et al produced fusion proteins comprising fragments of B19 capsid protein, and that neither reference teaches the native conformation of the B19 capsid. Collett et al confirms that the

recombinant fusion proteins lacked native epitopes. The examiner readily admits that Sisk et al, Cotmore et al, and Ozawa et al (T) would have been expected to produce proteins lacking conformational epitopes. However, these references are cited for their teachings of nucleic acids encoding B19 proteins. Dr. Spaan states his expert opinion that Wood et al is not relevant to claims 49-57 because canine parvovirus and human parvovirus are structurally quite dissimilar, citing as evidence two publications which were not available at the time the invention was made. These publications are therefore not evidence of the state of the art at the time the invention was made. Dr. Spaan states an opinion that, since there is no antigenic cross-reaction between canine and human parvovirus, the skilled worker would have had no basis to extrapolate on the use of B19 capsid proteins as vaccines or diagnostic agents. However, Ozawa et al (1988) points to several recognized similarities between B19 and other parvoviridae, including location of the capsid proteins on the right side of the genome, and states that "The dominance of the smaller capsid protein species is a consistent feature of the parvoviridae, suggesting that the appropriate ratio of capsid proteins is important for the assembly of these viruses".

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Chris Eisenschenk, can be reached on (703) 308-0452. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196 .

February 18, 1999

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1600